Circumventing antibiotic resistance in specialized hospital units

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Sanders and Sanders [1] introduced the idea of cycling antibiotics on special care units to circumvent the emergence of resistance in bacterial pathogens. The salient features of such an antibiotic cycling program, which include infection control procedures, elimination or avoidance of certain antibiotics and also continuous education and monitoring, were pointed out. As I understand the intention, the ideas presented in the paper were advanced to stimulate discussion, as no controlled trials were quoted to prove the efficacy of the strategy. Indeed, it might be difficult to devise a suitable control group.

What can happen to an antibiotic cycling program? To describe the worst scenario: within a few months of the introduction of such a cycling program, the staff will be disillusioned because nobody will remember which cycled regimen is in force, there being so many other tasks that have to be undertaken and regulated in intensive care units. It can also be foreseen that within a short period of time (less than 2 years of cycling), strains of multidrug-resistant *Pseudomonas aeruginosa* or *Enterobacter* spp., producing inducible β-lactamases and/or extended-spectrum β-lactamases with a loss or alteration of outer-membrane proteins, will invalidate this very mechanistic cycling process.

In my personal experience, there may be at least one other way to handle infections in patients on special care units to avoid or to postpone the emergence of resistance. Based upon results of microbiological investigations, it is possible to create not what is called in the paper an 'empirical' but rather a 'calculated' chemotherapy for different sites of infection, e.g. blood, lung, abdomen, wound, urinary tract.

The rules for such a calculated chemotherapy have to be elaborated co-operatively by clinicians, microbiologists and pharmacists, and have to take into account five different aspects: prevalence of pathogens at a given site of infection; susceptibility patterns of these pathogens; pharmacokinetic aspects, including dosing; the condition of the patient (e.g. immunosuppression, renal function); and costs. On the basis of these data, it is possible to create very different therapeutic regimens tailored to the special requirements—dictated by the local epidemiologic situation, the site of infection and the individual patient characteristics—which can be used in parallel, thus avoiding the impact of a single regimen over even a short period of time on selection of resistance. It is possible to use ureidopenicillins, second-generation cephalosporins, and in some cases third-generation cephalosporins, as well as aminoglycosides or potent fluoroquinolones such as ciprofloxacin. It is important to adapt the regimens to the local situation. For example, in many of the small or medium-sized hospitals in Germany, infections by methicillin-resistant *Staphylococcus aureus* (MRSA) are uncommon and emergence of resistance in MRSA to fluoroquinolones does not present so great a threat as it may do elsewhere.

During the time that the guidelines are in use, the results of culture must be monitored very carefully by the microbiologist on a continuous basis, to detect all possible resistance mechanisms in the pathogens isolated. This should be done in 'real time', to give early warning of the emergence of resistant strains. When this happens, it is time to change the guidelines of calculated chemotherapy. The analysis should show not only the susceptibilities of first isolates from individual patients but also those of subsequent isolates, to determine whether resistance may develop during treatment. A further point is the need for rapid microbiological results; for several years it has been possible in many cases to obtain full results within 24 h [2]. There are even some data showing that rapid microbiological results may improve survival of patients [3]. By introducing these methods, it is possible to shorten the period of calculated chemotherapy and to switch to individualized chemotherapy, eliminating carbapenems or third- and fourth-generation cephalosporins whenever possible. Rapid microbiology significantly decreases selective pressure by avoiding overuse of highly efficient antibiotics.

My personal opinion is that microbiologists should promote such varied therapeutic regimens in cooperation with clinicians and pharmacists. For future investigation I would propose to take patients on a regimen of calculated chemotherapy in combination with rapid microbiology as a control group to compare with a group of patients on wards which have adopted cycling therapy.

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Incidence of *Bilophila wadsworthia* in appendiceal, peritoneal and fecal samples from children

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In the course of their studies on appendicitis, Baron and coworkers recovered a new anaerobic rod, which was isolated from about 50% of the appendiceal samples from patients with complicated appendicitis and which was described in 1989 as *Bilophila wadsworthia* [1]. The lower intestinal tract seems to be the natural habitat of *B. wadsworthia*, where it was recovered from 60% of the subjects, with counts ranging from 3×10^3 to 2×10^8/g stool. Additionally, *B. wadsworthia* was isolated from 4% of saliva samples and from 3% of vaginal specimens from healthy volunteers [2]. Quite recently, *B. wadsworthia* has been described also in other infectious processes, such as scrotal abscess, mandibular osteomyelitis, pleural empyema and bacteremia, suggesting that *B. wadsworthia* is capable of acting as a pathogen [3–5]. There are no reports about the occurrence of *B. wadsworthia* in clinical specimens or in feces from children.

Included in this study were 229 children aged 3 months to 15 years, admitted to the department of pediatric surgery (University of Tübingen) during a 12-month period (6 January 1994 to 5 January 1995) because of acute abdominal pain in the right hypogastrium. Stool samples were taken from all patients. The main cause of abdominal pain was gastroenteritis (136 cases), but 51 of the children underwent appendectomy; in these patients the appendices were also studied. The appendices were divided lengthwise under sterile conditions for histopathologic and microbiological examination. According to the histopathologic findings and the visual assessment at surgery, seven cases were diagnosed as chronic appendicitis, 26 as acute or phlegmonous appendicitis and 14 as complicated (gangrenous or perforated) appendicitis. In four cases appendectomy was performed in the presence of abdominal pathology other than appendicitis (Table 1). In cases with suspicious intraoperative findings, peritoneal swabs were also examined (38 cases).

Table 1 Data on patients undergoing surgery

	Type of appendicitis			
	Negative	Chronic	Acute	Complicated
No.	4	7	26	14
Sex (M/F)	2/2	4/3	14/12	7/7
Mean age (years)	8.2	11.7	10.0	9.3
Mean WBC count at admission (per μL)	10190	9385	15134	17820
Mean temperature at admission (°C)	37.2	37.6	37.8	38.2

In stool samples the occurrence of *B. wadsworthia* only was investigated; from the appendix tissue only anaerobic isolates were recovered; and in peritoneal swabs aerobic and anaerobic organisms were isolated. The appendiceal samples were incubated on two Bacteroides–bile–esculin (BBE), brain–heart infusion (BHI) and kanamycin–vancomycin (KV) agar plates each. The peritoneal swab was used to inoculate plates of Columbia blood agar, Endo agar, BBE, BHI and KV agar and an enrichment broth. From each stool sample one loop was inoculated on two BBE plates. Media were incubated anaerobically (Anaerocult A, Merck) at 37 °C for at least 7 days. Blood and Endo agar plates were incubated aerobically at 37 °C for at least 48 h. The identification of *B. wadsworthia* was by the following methods: Gram stain; detection of bile resistance; positive catalase reaction (5% H_2O_2); short-chain fatty acid analysis (detection of acetate) by gas–liquid chromatography; negative reactions for glucose fermentation, esculin hydrolysis and indole production; positive reactions for H_2S production and nitrate reductase; and testing for urease activity.

Cultures of the appendices yielded 293 strains of more than 44 different anaerobic species (Table 2). *Bacteroides fragilis* (62.7%) and *B. wadsworthia* (50.9%) were the anaerobic species most often isolated from appendiceal samples, followed by *Bacteroides ovatus*, *Peptostreptococcus anaerobius*, *Peptostreptococcus micros* and *Prevotella intermedia*. The results presented showed marked similarities between non-inflamed and chronically inflamed appendices, in contrast to findings in acute and complicated appendicitis with respect to species and number of species of anaerobes recovered. Non-acutely inflamed appendices harbored on average four to five different anaerobic species, whereas in acute or complicated cases more than six different anaerobic species were identified. *B. wadsworthia* was recovered